

AMENDMENTS

Listing of Claims

The following listing of claims replaces all previous listings or versions thereof:

1. (Presently amended) A transgenic mouse, the cells of which comprise at least one endogenous altered LXR α allele, wherein said altered LXR α allele comprises the insertion of a selectable marker gene, that cannot express LXR α that responds to dietary cholesterol, wherein said mouse shows a phenotype of increased hepatic cholesterol accumulation when fed a 2% cholesterol diet for seven days compared to a control animal.
2. (Presently amended) The transgenic mouse of claim 1, wherein said cells comprise two endogenous altered LXR α alleles, wherein said altered LXR α alleles both comprise the insertion of a selectable marker gene that cannot express LXR α that responds to dietary cholesterol, and wherein said mouse shows a phenotype of hepatomegaly when fed a 2% cholesterol diet for ninety days.
3. (Canceled)
4. (Previously amended) The transgenic mouse of claim 1, wherein a transcript produced from said endogenous altered LXR α allele contains an interruption in the LXR α coding sequence.
5. (Previously amended) The transgenic mouse of claim 2, wherein a transcript produced from said endogenous altered LXR α alleles both contain an interruption in the LXR α coding sequences.

6. (Previously amended) The transgenic mouse of claim 1, wherein said endogenous altered LXR α allele contains a nonsense mutation that truncates the corresponding encoded LXR α polypeptide.
7. (Previously amended) The transgenic mouse of claim 2, wherein said endogenous altered LXR α alleles both contain a nonsense mutation that truncates the corresponding encoded LXR α polypeptide.
8. (Previously amended) The transgenic mouse of claim 1, wherein said endogenous altered LXR α allele contains a deletion of LXR α coding sequences.
9. (Previously amended) The transgenic mouse of claim 2, wherein said endogenous altered LXR α alleles both contain a deletion of LXR α coding sequences.
10. (Previously amended) The transgenic mouse of claim 1, wherein said endogenous altered LXR α allele contains a mutation in the 5' regulatory region of the LXR α gene.
11. (Previously amended) The transgenic mouse of claim 2, wherein said altered endogenous LXR α alleles both contain a mutation in the 5' regulatory region of the LXR α genes.
12. (Previously amended) The transgenic mouse of claim 10, wherein said alteration comprises substitution of an inducible/repressible promoter for the endogenous LXR α promoter.
13. (Previously amended) The transgenic mouse of claim 11, wherein said alterations comprise substitution of inducible/repressible promoters for both of the endogenous LXR α promoters.

14-20. (Canceled)

21. (Presently amended) A method for screening a candidate substance for the ability to reduce cholesterol levels via LXR α in a mammal comprising:

- (a) providing a transgenic mouse, the cells of which comprise at least one endogenous altered LXR α allele, wherein said altered LXR α allele comprises the insertion of a selectable marker gene that cannot express LXR α that responds to dietary cholesterol;
- (b) treating said mouse with said candidate substance; and
- (c) monitoring a cholesterol-related phenotype in said mouse,

wherein a reduction in said cholesterol-related phenotype in said mouse treated with said candidate substance, as compared to a similar mouse not treated with said candidate substance, indicates that said candidate substance reduces cholesterol levels via an LXR α -independent mechanism.

22. (Canceled)

23. (Original) The method of claim 21, wherein said phenotype is cholesterol absorption, circulating cholesterol, hepatic cholesterol, hepatomegaly, atherosclerosis, cardiac failure, cardiac (atrophy/hypertrophy), activity level, survival, cancer, reproduction, immune function, skin disease, cognitive function, and adrenal function.

24. (Previously amended) The method of claim 21, wherein said mouse is maintained on a high cholesterol diet.

25. (Previously amended) The method of claim 21, wherein said mouse further is treated with an agent that blocks cholesterol biosynthesis.

26. (Presently amended) The method of claim 21, wherein said cells comprise two endogenous altered LXR α alleles that cannot express LXR α that responds to dietary cholesterol, each allele comprising the insertion of a selectable marker gene.

27. (Presently amended) A method for screening a candidate substance for the ability to increase bile acid synthesis via LXR α in a mammal comprising:

- (a) providing a transgenic mouse, the cells of which comprise at least one endogenous altered LXR α allele, wherein said altered LXR α allele comprises the insertion of a selectable marker gene that cannot express LXR α that responds to dietary cholesterol;
- (b) treating said mouse with said candidate substance; and
- (c) monitoring a bile acid-related phenotype in said mouse,

wherein an increase in said bile acid-related phenotype in said mouse treated with said candidate substance, as compared to a similar mouse not treated with said candidate substance, indicates that said candidate substance increases bile acid synthesis via an LXR α -independent mechanism.

28. (Canceled)

29. (Original) The method of claim 27, wherein said bile acid-related phenotype is selected from the group consisting of cholesterol level, Cyp7a synthesis, fecal bile acid excretion, bile acid pool size and bile acid composition.

30-43. (Canceled)

44. (Presently amended) A transgenic mouse cell which comprises at least one endogenous altered LXR α allele, wherein said altered LXR α allele comprises the insertion of a selectable marker gene that cannot express LXR α that responds to dietary cholesterol.

45. (Presently amended) The transgenic cell of claim 44, wherein said cell comprises two endogenous altered LXR α alleles, wherein said altered LXR α alleles both comprise the

insertion of a selectable marker gene that cannot express LXR α that responds to dietary cholesterol.

46-58. (Cancelled)